Remarks

The Office Action mailed 14 August 2001 has been received and reviewed. Claims 12-16, 40, 42, 44, 46, 48, and 51 having been amended, the pending claims are claims 12-17, 39-49, and 51.

The specification has been amended at pages 48-51 with substitute sheets to correct the margins.

Claims 12-16, 40, 42, 44, 46, 48, and 51 have been amended to recite the full-length complements of the claimed primers. This amendment clarifies that the primers of claims 12-16, 40, 42, 44, 46, 48, and 51 are directed toward their full-length complement and not to complementary fragments or bases thereof.

Reconsideration and withdrawal of the objection and rejections are respectfully requested.

Objection to the Specification

Pursuant to the Examiner's request, enclosed herewith please find substitute sheets (pages 48-51) of the specification as filed. The substitute sheets are provided to amend the margins on pages 48-51 of the specification. As Applicants have amended the margins of pages 48-51 of the specification, the Examiner's objection is rendered moot. Accordingly, withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. §102

Claims 12-16 were rejected under 35 U.S.C. §102(b) as being anticipated by Leegaard et al. (APMIS, 104, 302-306 (1996)). Claims 12-17 and 39-48 were rejected under 35 U.S.C. §102(a) as being anticipated by Vahaboglu et al. (J. Clin. Microbiology, 36(3):827-829 (March 1998)). Claims 12-17 and 39-48 were rejected under 35 U.S.C. §102(a) as being anticipated by Speldooren et al. (Antimicrobial Agents and Chemotherapy, 42(4):879-884 (April 1998)). Claims 12-17 and 39-48 were rejected under 35 U.S.C. §102(a) as being anticipated by Siu et al. (APMIS, 106, 917-920 (September 1998)). These rejections are respectfully traversed.

Leegaard et al. teach the detection of the OXA-1 and TEM-1 genes from antibiotic resistant *Salmonella* strains isolated from the blood of patients with fever in Kenya and Malawi. Profiles of the OXA-1 and TEM-1 genes were determined microbiologically using the disc diffusion test (page 303, left column, 3rd full paragraph). However, only the TEM-1 gene was subjected to further analysis by PCR (page 882, left column).

Vahaboglu et al. teach the detection and identification of ceftazidime-hydrolyzing extended-spectrum mutants of OXA-10 β-lactamase (page 827). Vahaboglu et al. further teach a method to detect OXA-10 enzymes and their OXA-10 ceftazidime-hydrolyzing extended spectrum derivatives using PCR (page 827, left column). Specifically, "PCR was designed to amplify a 720-bp fragment of the OXA-10, -17, -11, -14, and -16 genes with the sense primer OPR1 (5'-GTCTTTCGAGTACGGCATTA-3') at position 35 and the antisense primer OPR2 (5'-ATTTTCTTAGCGGCAACTTAC-3') at position 755 of bla_{OXA-10}" (pages 827 and 828).

Speldooren et al. teach a single-stranded conformation polymorphism (SSCP)-PCR method to differentiate the genes encoding inhibitor-resistant β-lactamases in eight clinical isolates (*Escherichia coli* isolates obtained from Ambroise-Paré Hospital between 1993 and 1994) resistant to amoxicillin-clavulanic acid using 3 bla_{TEM} primer pairs (Abstract and page 880 under the heading Clinical isolates). Speldooren et al. further teach that the TEM primers did not produce an amplification product in a lysate only possessing the OXA gene, but that OXA-1 primers were able to produce amplification products of the OXA-1 gene (page 882, left column).

Siu et al. teach the correlation between *in vitro* susceptibility results for amoxicillin-clavulanate (AMC) and ampicillin-sulbactam (SAM) from studying 136 clinical and control strains of *Enterobacteriaceae* harboring TEM-1, SHV-1, or OXA-1-like β-lactamases (Abstract). Siu et al. further teach that the use of a primer set known to be specific for bla_{OXA-1} and bla_{OXA-4} were able to PCR amplify the gene encoding the OXA-1-like enzyme (page 917 under the heading β-lactamase characterization).

In rejecting the claims the Examiner noted in every instance that at least one base in the primers taught by the cited documents was complementary with SEQ ID NOs:34-43.

As the primers of the present invention (SEQ ID NOs:34-43) are novel and claims 12-16, 40, 42, 44, 46, 48, and 51 have been amended to recite "full length complements thereof," Applicants submit that the claims no longer read on art teaching a single base or fragment complementary to the primers of the present invention. Thus, Applicants have rendered the Examiner's rejection moot.

In the Office Action, the Examiner addressed the claims with specific sequences. There are no comments as to the claims without specific sequences, such as claims 17, 39, 41, 43, 45, 47, and 49. Thus, the rejection is not fully understood.

With respect to claims 17, 39, 41, 43, 45, 47, and 49, Applicants submit that the cited documents fail to teach all of the elements of Applicants' claimed invention. Independent claim 17, from which claims 39, 41, 43, 45, and 47 depend, and claim 49 are directed towards a valuable screening method and diagnostic kit for identifying a beta-lactamase family in a clinical sample to enable clinicians to better treat a bacterial infection. In contrast, at most, the prior art teaches a method of detecting specific members of a beta-lactamase family. It is respectfully submitted that the selection of primers that are specific for identifying a general beta-lactamase family is not a routine or trivial matter. A significant amount of creativity and experimental evaluation goes into the selection of primers that are specific for a general beta-lactamase family, as opposed to just one member of a family. As the cited documents teach primers for specific members of an OXA family of beta-lactamase enzymes, they fail to teach the present invention's novel contribution to the art. That is, there is no teaching or suggestion that such primers could be used in a screening assay or diagnostic kit of general diagnostic utility. Thus, the cited documents do not anticipate claims 17, 39, 41, 43, 45, 47, and 49 of the present invention.

For the above reasons, Applicants respectfully submit that the invention recited in claims 21-17 and 39-48 is patentable over the cited documents. Accordingly,

reconsideration and withdrawal of the rejections of claims 12-17 and 39-48 under 35 U.S.C. §102(a) and claims 12-16 under 35 U.S.C. §102(b) are respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claims 49 and 51 were rejected under 35 U.S.C. §103(a) as unpatentable over Vahaboglu et al. (J. Clin. Microbiology, 36(3):827-829 (March 1998)) as applied to claims 12-17 and 39-48, and further in view of Fluit et al. (WO 91/08305 (June 13, 1991)). In order to expedite the prosecution of the above-identified patent application, Applicants have canceled claim 51 and have incorporated its contents into claim 49. This rejection is respectfully traversed as it applies to claim 49, as amended.

In rejecting claims 49 and 51 the Examiner stated that "it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized the components and method taught by Vahaboglu et al., into a kit because the method for identifying a beta-lactamase in a clinical sample using PCR was known at that time the inventions were made and the kit format was utilized not only assemble a variety of different reagents together but ensured the quality and compatibility of the reagents" (page 5 and 6 of the Office Action).

Claim 49 is directed toward a diagnostic kit for detecting an OXA-family beta-lactamase. Claim 51, which depends from claim 49, sets forth a specific list of primers (SEQ ID NOs:34-43 and full-length complements thereof) to be used in an OXA-family beta-lactamase.

Vahaboglu et al. is discussed above.

Fluit et al. teach a diagnostic test kit for the detection of *Staphylococcus* bacteria that are resistant to methicillin and related penicillins insensitive to β-lactamase in a sample by means of PCR analysis. The kit includes a DNA primer set, as well as one or more further means required for PCR analysis, such as a polymerase a polymerase, a polymerization liquid, an oil overlay, a reaction vessel and means for detecting the amplified DNA (page 8, lines 3-10).

Applicants respectfully traverse this rejection for a number of reasons. Establishment of a *prima facie* case of obviousness requires that the cited document(s) teach or suggest all of the limitations of the rejected claims. In addition, some suggestion or motivation must be provided to modify the document to reach the claimed invention.

It is well accepted under §103(a) that to render an invention obvious, the available prior art must contain a suggestion to make the claimed composition or device, and carry out the claimed process with a reasonable expectation of success.

Applicants submit that as the cited documents fail to teach a diagnostic kit for detecting all members of the OXA-family beta-lactamase, the cited documents fail to teach or suggest the claimed invention as recited in claims 49 and 51. Furthermore, with respect to claim 51, as the listed primers and their corresponding full-length complements are novel, one of skill in the art would not be able to carry out the claimed diagnostic kit with a reasonable expectation of success.

As the cited documents do not teach or suggest all of the elements of the diagnostic kit as claimed by Applicants, the documents fail to render Applicants' invention obvious.

For the above reasons, Applicants respectfully submit that the invention recited in claims 49 and 51 is patentable over the cited documents. Accordingly, reconsideration and withdrawal of the rejection of claim 49 under 35 U.S.C. §103(a) are respectfully requested.

Summary

It is respectfully submitted that the pending claims 12-17, 39-49, and 51 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for

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